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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/776,190	01/24/97	JOSEL H	P564-7002

EXAMINER

HM12/0509

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ART UNIT	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

Office Action Summary	Application No. 08/776,190	Applicant(s) Josel et al.
	Examiner G. Hsu	Art Unit 1627

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Feb 15, 2001* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *72-89 and 100-102* is/are pending in the application.

4a) Of the above, claim(s) *78, 79, 82, 89, and 102* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *72-77, 80, 81, 83-88, 100, and 101* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☒ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☒ All b) ☐ Some* c) ☐ None of:

1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

Change of Examiner

1. **Please Note:** There is a change in Examiner handling prosecution in the current case from Examiner J. Ricigliano to Examiner G. Hsu.

Status of Application

2. A Petition For a 3 Month Extension of Time, An Amendment and Reply Under 37 C.F.R. 1.111 and A Change of Correspondence Request, respectively received February 15, 2001, were entered as Paper Nos. 24-25.

Status of the Claims

3. Claims 72-89 and 100-102 (claims 100-102 are newly added) are pending in the current application.

4. Claims 72-77, 80-81, 83-88 and 100-101 are under examination in the current application.

5. Claims 78, 79, 82 and 89 were withdrawn from further consideration by the Examiner under 37 C. F. R. 1.142(b), as being drawn to a non-elected inventions, the requirement having been traversed in Paper No. 22.

6. Claims 1-71 and 90-99 are canceled as per applicants' March 5, 1998, August 19, 1998, August 31, 1999 and February 15, 2001 requests.

Election/Restriction

7. For the record, it is reiterated that applicants':

[1] election with traverse of Group I, claims 72-89; and
[2] election of the following sub-species:
    [a] subspecies A: amino acids;
    [b] subspecies B: hormones; and
    [c] subspecies C: luminescent metal chelates

for examination purposes was acknowledged in a previous office action.

8. Claim 102 is withdrawn from further consideration by the Examiner under 37 C.F.R. 1.142(b), as being drawn to a non-elected inventions, the requirement having been traversed in Paper No. 22.

Newly added claim 102 is drawn to a nucleotide analogue, which is drawn to non-elected species (see, applicants' remarks in Paper No. 22).

Response to February 15, 2001 Amendment and Reply Under 37 C.F.R. 1.111

9. Applicants' arguments filed in the February 15, 2001 Amendment and Reply have been fully considered and discussed below, under each corresponding section heading.

10. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawn Objection(s) and/or Rejection(s)

11. The rejections of claims 72-77, 80-81, 83-88 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention are withdrawn in light of applicants' arguments and/or amendments.

12. The rejection of claims 72, 86 and 87 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had

possession of the claimed invention are withdrawn in light of applicants' arguments and/or amendments.

13. The rejections of claims 72-77, 80-81, 83-88 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention withdrawn in light of applicants' arguments and/or amendments.

Outstanding Objection(s) and/or Rejection(s)

Note: **For applicants' convenience, in the following section the record is reiterated below in its entirety.**

Claim Rejections - 35 USC § 102

14. The rejection of claims 72-77, 80-81, 83-88 and 100-102 (formerly directed to claims 72, 74-77, 80-81, 83 and 86) under 35 U.S.C. 102(b) as being anticipated by Bredehorst et al [Analytical Biochemistry 193(2) 272-278] are maintained for the following reasons of record.

Bredehorst et al teach insulin (a polymeric carrier having 2 amino acids) conjugated to a dinitrophenol (DNP) group and three fluorescein molecules coupled to reactive side groups (carboxyl or amine) all at predetermined positions. Therefore, Bredehorst et al anticipate the invention of claims 72, 74-77, 80-81. As the carrier has negatively charged sulfate groups it anticipates claim 83. As the molecular weight of DNP is in the range of 100-2000 Daltons claim 86 is anticipated.

Note that the statement "wherein the polymeric carrier is prepared by synthesis on a solid phase" does not limit the product as it is directed to a process of making rather than the product and the product can be made by other routes than solid phase synthesis.

15. Applicants' arguments filed 5/30/200 have been fully considered but they are not persuasive.

Applicants assert that because the claims recite the polymeric carrier is synthetically-made Bredehorst et al does not read on the instant claims. This argument has been considered but is not found persuasive as the argument is directed to the process of preparation not the product made. As the product of Bredehorst et al reads on all of the limitations of the rejected claims it anticipates the product set forth in those claims. Therefore, the rejection is maintained for the reasons above and for the reasons of record.

In the February 15, 2001 Amendment and Reply Under 37 C.F.R. § 1.111, applicants assert that:

[1] claim 72, which has been amended to recite the following limitation, wherein "the carrier is non-immunologically reactive when the monomeric units are amino acids" and claims 74-77, 80-81, 83 and 86 (which depend from claim 72), now distinguishes the claimed invention from the prior art; and

[2] based upon the foregoing, requests reconsideration of the above-identified rejection.

In response it is the position of the Examiner that:

[1] applicant's arguments have been considered, found unpersuasive in light of the new matter rejections set forth below under New Grounds of Rejection section; and

[2] **in light of the foregoing, the rejection of record is maintained and deemed proper.**

16. The rejection of claims 72-77, 80-81, 83-88 and 100-101 (formerly directed to claims 72, 74-77, 80-81, 83 and 86) under 35 U.S.C. 103(a) as being unpatentable over Bredehorst et al in view of Bard et al.[US 5,310,687] are maintained for the following reasons of record.

See the teaching of Bredehorst et al *supra.*

Bredehorst et al do not teach the use of luminescent metal chelates as required in an alternative embodiment in claim 81, or as a specific limitation of claims 73 and 84.

However, Bard et al teach the use of luminescent metal chelates as a marker with superior properties for use in assays (See the summary of the invention starting in column 5).

It would have been prima facia obvious to one of ordinary skill in the art at the time the invention was made use the luminescent metal chelates of Bard et al et al in the conjugates as taught Bredehorst et al because Bredehorst et al teach the incorporation of detectable marker groups into conjugates for immuno assays and Bard et al teach the incorporation of luminescent metal chelates into molecules for detecting analyte in immuno assays formats. One of ordinary skill in the art would have been motivated to incorporate the luminescent metal chelates of Bard et al in conjugates as taught by Bredehorst et al in order to take advantage of the rapid efficient and sensitive detection permitted by the chemiluminescent markers taught by Bard et al (see abstract). One of ordinary skill in the art would reasonably have expected to be successful because Bard et al had previously incorporated and applied the chemiluminescence metal chelates to a variety of assays including immunoassay.

In the February 15, 2001 Amendment and Reply Under 37 C.F.R. § 1.111, applicants assert that:

[1] claim 72, which has been amended to recite the following limitation, wherein "the carrier is non-immunologically reactive when the monomeric units are amino acids" and claims 74-77, 80-81, 83 and 86 (which depend from claim 72), now distinguishes the claimed invention from the prior art; and

based upon the foregoing claim amendments, there is no suggestion or motivation to combine the references; and

[2] in light of the foregoing, requests reconsideration of the above-identified rejection.

In response it is the position of the Examiner that:

[1] applicant's arguments have been considered, found unpersuasive in light of the new matter rejections set forth below under New Grounds of Rejection section; and

[2] **in light of the foregoing, the rejection of record is maintained and deemed proper.**

17. The rejection of claims 72-77, 80-81, 83-88 and 100-101 (formerly directed to claims 72, 74-77, 80-81, 83 and 86) under 35 U.S.C. 103(a) as being unpatentable over Buchardt *et al* WO 92/20703 in view of Bredehorst *et al* (Analytical Biochemistry 193:272-279) are maintained for the following reasons of record.

Buchardt *et al* teach the synthesis and use of peptide nucleic acids or PNA (which reads on nucleotide analogs and amino acids as each monomeric unit of a PNA is an amino acid) wherein the PNA is at made of at least 2 monomers (page 5 line 2), and in a preferred embodiment the length is from 2-61 (page 7 line 10). Buchardt *et al* teach that PNA molecules

may be conjugated to reporter ligands including: alkylators, fluorescent compounds, spin labels or protein recognition ligands such as biotin or haptens, which read on marker groups, haptens or solid phase binding groups coupled to reactive side chains (page 20 starting at line 26). Moreover, Buchardt *et al* teach that the L groups (see figure III page 3 for example), which read on groups coupled to reactive side chains, can be a fluorophore, radio or spin label or protein-recognizing ligand such as biotin or a hapten (page 19 lines 5-8). In that each L group is specifically located on the molecule in a location which is determined by the synthetic process under the control of the researcher these groups must be at predetermined positions.

With respect to the dependent claims Buchardt *et al* teach that the oligomers of their invention can be from 2-61 monomers (see page 7, structure III and line 10) which reads on the limitations of claims 74 and 75. In that L groups are explicitly recited as being haptens or fluorophores and as many as 61 L groups are present in a recited preferred embodiment, Buchardt *et al* meet the limitations of claims 76-77. As the terminal groups of the PNA molecules can be acids or amines the reference reads on the limitation of claim 83. Buchardt *et al* teach that the molecule of their invention may be used in a method of capturing a nucleic in a hybridization assay (page 9 line 14 to page 10 line 36), thus the conjugate must be capable of forming a double strand helix and reads on the limitation of claim 85. Buchardt *et al* teach that the molecules of their invention can be conjugated to a peptide s where the peptides have signaling activity which renders obvious the peptide hormones or peptide epitopes as required by the invention of claim 88.

Buchardt *et al*, while teaching that multiple groups may be incorporated into or conjugated to a PNA molecule, does not explicitly recite incorporating both marker groups and haptens or solid phase binding groups into a single polymeric conjugate molecule.

However, Bredehorst *et al* teach the formation of carrier molecules (conjugates) formed from amino acids with both hapten and multiple marker molecules placed at specific positions see figure 1. Bredehorst et al also specifically recite the incorporation of negatively charge groups (i.e., SO3-, see figure 1) and the use of amino acid based conjugates and Buchardt et al teach the attachment of positive charged (polylysine) and negative charged (carboxyl or sulfo groups) to the carrier molecule; page 20 lines 17-25 which also read further on the limitations of claim 83.

It would have been *prima facia* obvious to one of ordinary skill in the art at the time the invention was made to incorporate both hapten and marker molecules as taught by Bredehorst *et al* in a PNA which is a peptide (and a nucleic acid analog) as taught by Buchardt *et al* because Buchardt *et al* teach the incorporation of haptens and markers into PNA molecules at selected sites and Bredehorst *et al* teach that is it known in the art to incorporate both a hapten and a marker into the same conjugate. One of ordinary skill in the art would have been motivated to do so in order to provide for a sensitive immuno assay of haptens which can quench the fluorophore markers without loss of sensitivity as taught by Bredehorst *et al*. One of ordinary skill in the art would have reasonably expected to be successful because the successful synthesis of PNA molecules incorporating multiple functionalities at specific positions and the incorporation haptens or markers had previously been taught by Buchardt *et al* and the required placement of a

hapten at a position distant enough to prevent quenching of the marker fluorophore would be readily achieved with a PNA molecule.

18. Applicants' arguments filed 8/31/1999 have been fully considered but they are not persuasive. Applicants' have argued that the claims now delete reference to PNA molecules and hence the rejections over Buchardt are moot. This argument is not found persuasive as PNA molecules are comprised of amino acids and hence the reference is still applicable to the instant claims.

In the February 15, 2001 Amendment and Reply Under 37 C.F.R. § 1.111, applicants assert that:

[1] claim 72, which has been amended to recite the following limitation, wherein "the carrier is non-immunologically reactive when the monomeric units are amino acids" and claims 74-77, 80-81, 83 and 86 (which depend from claim 72), now distinguishes the claimed invention from the prior art; and

based upon the foregoing claim amendments, there is no suggestion or motivation to combine the references; and

[2] in light of the foregoing, requests reconsideration of the above-identified rejection.

In response it is the position of the Examiner that:

[1] applicant's arguments have been considered, found unpersuasive in light of the new matter rejections set forth below under New Grounds of Rejection section; and

[2] **in light of the foregoing, the rejection of record is maintained and deemed proper.**

19. The rejection of claims 72-77, 80-81, 83-88 and 100-101 (formerly directed to claims 72, 74-77, 80-81, 83 and 86) under 35 U.S.C. 103(a) as being unpatentable over Buchardt et al in

view of Bredehorst and further in view of Bard et al.[US 5,310,687] are maintained for the following reasons of record.

See the teaching of Buchardt et al in view of Bredehorst et al supra.

Buchardt et al in view of Bredehorst et al do not teach the use of luminescent metal chelates as required in an alternative embodiment in claim 81, or as a specific limitation of claims 73 and 84.

However, Bard et al teach the use of luminescent metal chelates as a marker with superior properties for use in assays (See the summary of the invention starting in column 5).

It would have been prima facia obvious to one of ordinary skill in the art at the time the invention was made use the luminescent metal chelates of Bard et al et al in the conjugates as taught by Buchardt et al in view of Bredehorst et al because Buchardt et al in view of Bredehorst et al teach the incorporation of marker groups into conjugates for immuno assays and Bard et al teach the incorporation of luminescent metal chelates into molecules for detecting analyte in immuno assays formats. One of ordinary skill in the art would have been motivated to incorporate the luminescent metal chelates of Bard et al in conjugates as taught by Buchardt et al in view of Bredehorst et al in order to take advantage of the rapid efficient and sensitive detection permitted by the chemiluminescent markers taught by Bard et al (see abstract). One of ordinary skill in the art would reasonably have expected to be successful because Bard et al had previously incorporated and applied the chemiluminescence metal chelates to a variety of assays including immunoassay.

In the February 15, 2001 Amendment and Reply Under 37 C.F.R. § 1.111, applicants assert that:

[1] claim 72, which has been amended to recite the following limitation, wherein "the carrier is non-immunologically reactive when the monomeric units are amino acids" and claims 74-77, 80-81, 83 and 86 (which depend from claim 72), now distinguishes the claimed invention from the prior art; and

based upon the foregoing claim amendments, there is no suggestion or motivation to combine the references; and

[2] in light of the foregoing, requests reconsideration of the above-identified rejection.

In response it is the position of the Examiner that:

[1] applicant's arguments have been considered, found unpersuasive in light of the new matter rejections set forth below under New Grounds of Rejection section; and

[2] **in light of the foregoing, the rejection of record is maintained and deemed proper.**

New Grounds of Rejection

20. **Note that: the following new grounds of rejection are:**

Section I: necessitated by applicants' amendments; and

Section II: not necessitated by applicants' amendments.

Section I: New Grounds of Rejection Necessitated By Applicants' Amendments

New Matter

21. Claims 72, 82-83 and 100 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey

to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The added material of the following amended claims, which are not supported by the original disclosure is as follows:

the specification **does not teach** the recitation of the terms as indicated below in ***bold***:

[1] **"wherein the carrier is non-immunologically reactive when the monomeric units are amino acids (i.e., see claim 72)"**;

[2] **"a charged group selected from the group consisting of positively charged groups and negatively charged groups (i.e., see claims 83 and 84)"**; and

[3] **"wherein the reactive side groups coupling the hapten molecules and the reactive side groups coupling the marker groups or solid phase binding groups are alike (i.e., see claim 101)."**

Accordingly, there is lack of descriptive support for the above-identified terms, wherein the components, substituents, elements, etc. of the claimed invention are other than those recited supra.

In accordance with M.P.E.P. Section 714.02, applicants should specifically point out support for any amendments made to the instant disclosure.

Applicants are required to cancel the new matter in the reply to this Office action.

Claim Rejections - 35 USC § 112

22. The following is a quotation of the first and second paragraphs of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to

> make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.
>
> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

23. Claims 100-101 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a conjugate comprising:

[a] a synthetic polymeric carrier of "a polyamide backbone made of the same or different monomeric units of the formula $(CH_2)_k$-CHR'-N[CO-$(CH_2)_i$-L]-CH_2-$(CH_2)_m$-NH-CO- " (i.e., e.g., see instant specification at page 7, lines 1-27) having a maximum of 100 monomeric units selected from the group consisting of nucleotides and amino acids;

[b] 1-10 hapten molecules (as in claim 101) and/or 2-10 hapten molecules (as in claim 102) (i.e., e.g. see instant specification at page 8, lines 1-33);

[c] 1-10 marker groups (see, instant specification at page 9, lines 3-4 and page 9, lines 13-31 to page 11, lines 1-17 and page 12, lines 22-24); or

[d] solid phase binding groups (i.e., e.g., see, instant specification at page 12, lines 18-22)

[e] coupled to reactive side groups (i.e., e.g. see, the instant specification at page 9, lines 9-15, which states "wherein the hapten molecules and marker or solid phase binding groups are preferably coupled to the carrier chain via reactive amino or/and thiol side groups particularly preferably via reactive primary amino side groups";

[f] at predetermined positions on the polymeric carrier (i.e., e.g., "primary amino side groups that are located at positions of the peptide at which is intended to introduce a hapten . . ., etc."; see, instant specification at page 15, lines 9-14);

but does not reasonably provide enablement for ***all*** conjugate comprising: ***all*** synthetic polymeric carriers; ***all*** hapten molecules, ***all*** marker groups, ***all*** solid phase binding groups, coupled to ***all*** reactive side groups at ***all*** predetermined positions on the polymeric carrier. The specification

does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Factors considered in making such determinations are set forth in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). As discussed below, those factors include, but are not limited to, the: (1) breadth of the claims; (2) nature of the invention; (3) state of the prior art; (4) level of one of ordinary skill; (5) level of predictability in the art; (6) amount of direction provided by the inventor; (7) existence of working examples; and (8) quantity of experimentation needed to make or use the invention cased on the disclosure content.

In the present case, [1] the breadth of the claims encompass a conjugate comprising a synthetic polymeric carrier having a maximum of 100 monomeric units selected from the group consisting of 1-10 or 2-10 hapten molecules and 1-10 marker groups or solid phase binding groups, wherein the hapten molecules and the marker groups or solid phase binding groups are coupled to reactive side groups at predetermined positions on the polymeric carrier. However, the examples in the specification teach the use of specific synthetic polymeric carriers with a specific monomeric unit formula (i.e., as defined above and in the instant specification at page 7, lines 1-27) selected from the group consisting of 1-10 or 2-10 hapten molecules and 1-10 marker groups or solid phase binding groups, wherein the hapten molecules and the marker groups or solid phase binding groups are coupled to reactive side groups at predetermined positions on the polymeric carrier to yield positive or negative results; [2] the nature of the invention cannot be determined in light of the foregoing and without knowing the exact components that comprise the claimed conjugate to be used in the instant invention; [3] and [5] the state of the art and the level

of predictability in the art cannot be predicted with any certainty what specific components that form the claimed conjugates and/or what specific conjugates should be used and are likely to provide productive results beyond those examples taught in the specification; [4] and [6] the inventor provides no guidance beyond the examples of conjugates and/or corresponding components taught in the specification as previously mentioned. As a result one of ordinary skill in the art could not predict what other types of conjugates and/or corresponding components may be used in the claimed invention; and [7] and [8] while the existence of working examples are limited to Examples 1-4 (i.e., see instant specification at pages 22-28), an indeterminate quantity of experimentation would be necessary to determine all conjugates and/or all conjugate components of the claimed invention.

In light of the preceding discussion, one skilled in the art ***could not practice*** the claimed invention ***without undue experimentation,*** as claims 100 and 101 fail to correlate reasonably with either the enabling disclosure of the specification and the claims.

24. Claims 72 and 100-101 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

25. Claim 72 is vague and indefinite in that the following terms are not defined:

[1] "wherein the carrier is non-immunologically reactive when the monomeric units are amino acids"; it is unclear what the aforementioned term refers to, as the metes and bounds of the aforementioned claim cannot be determined as the specification, claims and art do not recognize

what the generic term "non-immunologically reactive" defines; applicants are requested to point to where in the specification that term is defined. Clarification is requested.

26. Claim 100 is vague and indefinite in that the following terms are not defined:

[1] "the conjugate containing 2-10 hapten molecules and 1-10 marker groups or solid phase binding groups, wherein the hapten molecules and the marker groups or solid phase binding groups are coupled to reactive side groups at predetermined positions on the polymeric carrier"; it is unclear what the aforementioned term refers to, as the metes and bounds of the aforementioned claim cannot be determined as the specification, claims and art do not recognize what the generic terms: [a] "predetermined positions on the polymeric carrier" refers to; and/or [b] whether the phrase the conjugate containing "2-10 hapten molecules and 1-10 marker groups or solid phase binding groups" indicates **either** "2-10 hapten molecules and 1-10 marker groups" **or** "solid phase binding groups" **or instead** indicates "2-10 hapten molecules" **and** "1-10 marker groups or solid phase binding groups" (i.e., e.g., the instant specification at page 5, lines 25-28, states that "when using the conjugate according to the invention that contain 1-10 hapten molecules **and** a defined number of marker or solid phase binding groups as antigens . . . "); applicants are requested to point to where in the specification that term is defined. Clarification is requested.

27. Claim 101 is vague and indefinite in that the following terms are not defined:

[1] "the conjugate containing 2-10 hapten molecules and 1-10 marker groups or solid phase binding groups, wherein the hapten molecules and the marker groups or solid phase binding groups are coupled to reactive side groups at predetermined positions on the polymeric carrier and wherein the reactive side groups coupling the hapten molecules and the reactive side groups

coupling groups or solid phase binding groups are alike"; it is unclear what the aforementioned term refers to, as the metes and bounds of the aforementioned claim cannot be determined as the specification, claims and art do not recognize what the generic terms: [a] "predetermined positions on the polymeric carrier" refers to; [b] whether the phrase the conjugate containing "2-10 hapten molecules and 1-10 marker groups or solid phase binding groups" indicates **either** "2-10 hapten molecules and 1-10 marker groups" **or** "solid phase binding groups" **or instead** indicates "2-10 hapten molecules" **and** "1-10 marker groups or solid phase binding groups" (i.e., e.g., the instant specification at page 5, lines 25-28, states that "when using the conjugate according to the invention that contain 1-10 hapten molecules **and** a defined number of marker or solid phase binding groups as antigens . . . "); and/or [c] what determines that reactive side groups coupling the hapten molecules and the reactive side groups coupling groups or solid phase binding groups **"are alike"** (i.e., e.g., the instant specification, Example 3 at page 6, lines 1-11 depicts in that specific example and not in every case, that the metal chelate and hapten molecules are coupled to the peptide chain via the ε-amino side group of the lysines); applicants are requested to point to where in the specification that term is defined. Clarification is requested.

Section II: New Grounds of Rejection Not Necessitated By Applicants' Amendments

Specification

28. The disclosure is objected to because of the following informalities.

29. A reference to the prior application must be inserted as the first sentence of the specification of this application if applicant intends to rely on the filing date of the prior application under 35 U.S.C. 119(e) or 120. See, 37 CFR 1.78(a).

The instant application does not refer to PCT/EP 95 Application Serial No. 02915, Filed on July 24, 1995, from which the instant application derives priority as a U.S. 371 application and the following foreign applications, Federal Republic Germany Applications: P 4426276.0, Filed: July 25, 1994; P 4430998.8, Filed: August 31, 1994; P 4430973.2, Filed: August 31, 1994; and P 4439345.8, Filed: November 4, 1994 from which the instant application derives priority under the specification heading entitled "Related Applications." Appropriate correction is requested.

30. Claims 72 and 87 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a conjugate comprising:

[a] a synthetic polymeric carrier of "a polyamide backbone made of the same or different monomeric units of the formula $(CH_2)_k$-CHR'-N[CO-$(CH_2)_i$-L]-CH_2-$(CH_2)_m$-NH-CO- " (i.e., e.g., see instant specification at page 7, lines 1-27) having a maximum of 100 monomeric units selected from the group consisting of nucleotides and amino acids;

[b] 1-10 hapten molecules (i.e., e.g., see specific hapten molecules in instant specification at page 8, lines 1-33);

[c] 1-10 marker groups (i.e., e.g., see specific marker groups in instant specification at page 9, lines 3-4 and page 9, lines 13-31 to page 11, lines 1-17 and page 12, lines 22-24); or

[d] solid phase binding groups (i.e., e.g., see, specific solid phase binding groups in instant specification at page 12, lines 18-22)

[e] coupled to reactive side groups (i.e., e.g. see, specific reactive side groups in instant specification at page 9, lines 9-15, which states "wherein the hapten molecules and marker or solid phase binding groups are preferably coupled to the carrier chain via reactive amino or/and thiol side groups particularly preferably via reactive primary amino side groups";

[f] at predetermined positions on the polymeric carrier (i.e., e.g., see specific positions, such as "primary amino side groups that are located at positions of the

peptide at which is intended to introduce a hapten . . ., etc."; see, instant specification at page 15, lines 9-14); and

[g] the conjugate as in claim 86, wherein the hapten molecules are pharmacological active substances (i.e., e.g., see specific substances in instant specification at page 8, lines 3-18)

but does not reasonably provide enablement for ***all*** conjugate comprising: ***all*** synthetic polymeric carriers; ***all*** hapten molecules, ***all*** marker groups, ***all*** solid phase binding groups, coupled to ***all*** reactive side groups at ***all*** predetermined positions on the polymeric carrier and/or ***all*** pharmacologically active substances. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Factors considered in making such determinations are set forth in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). As discussed below, those factors include, but are not limited to, the: (1) breadth of the claims; (2) nature of the invention; (3) state of the prior art; (4) level of one of ordinary skill; (5) level of predictability in the art; (6) amount of direction provided by the inventor; (7) existence of working examples; and (8) quantity of experimentation needed to make or use the invention cased on the disclosure content.

In the present case, [1] the breadth of the claims encompass a conjugate comprising a synthetic polymeric carrier having a maximum of 100 monomeric units selected from the group consisting of 1-10 or 2-10 hapten molecules and 1-10 marker groups or solid phase binding groups, wherein the hapten molecules and the marker groups or solid phase binding groups are coupled to reactive side groups at predetermined positions on the polymeric carrier and/or hapten

molecules selected from pharmacologically active substances. However, the examples in the specification teach the use of specific synthetic polymeric carriers with a specific monomeric unit formula (i.e., as defined above and in the instant specification at page 7, lines 1-27) selected from the group consisting of 1-10 or 2-10 hapten molecules and 1-10 marker groups or solid phase binding groups, wherein the hapten molecules and the marker groups or solid phase binding groups are coupled to reactive side groups at predetermined positions on the polymeric carrier and/or pharmacologically active substances (i.e., e.g., see specification pages as set forth above) to yield positive or negative results; [2] the nature of the invention cannot be determined in light of the foregoing and without knowing the exact components that comprise the claimed conjugate to be used in the instant invention; [3] and [5] the state of the art and the level of predictability in the art cannot be predicted with any certainty what specific components that form the claimed conjugates and/or what specific conjugates should be used and are likely to provide productive results beyond those examples taught in the specification; [4] and [6] the inventor provides no guidance beyond the examples of conjugates and/or corresponding components taught in the specification as previously mentioned. As a result one of ordinary skill in the art could not predict what other types of conjugates and/or corresponding components may be used in the claimed invention; and [7] and [8] while the existence of working examples are limited to Examples 1-4 (i.e., see instant specification at pages 22-28), an indeterminate quantity of experimentation would be necessary to determine all conjugates and/or all conjugate components of the claimed invention.

In light of the preceding discussion, one skilled in the art ***could not practice*** the claimed invention ***without undue experimentation,*** as claims 72 and 87 fail to correlate reasonably with either the enabling disclosure of the specification and the claims.

31. Claim 72 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

32. Claim 72 is vague and indefinite in that the following terms are not defined:

[1] "the conjugate containing 1-10 hapten molecules and the marker groups or solid phase binding groups, wherein the hapten molecules and the marker groups or solid phase binding groups are coupled to reactive side groups at "predetermined positions on the polymeric carrier"; it is unclear what the aforementioned term refers to, as the metes and bounds of the aforementioned claim cannot be determined as the specification, claims and art do not recognize what the generic terms: [a] "predetermined positions on the polymeric carrier" refers to; and/or [b] whether the phrase the conjugate containing "1-10 hapten molecules and 1-10 marker groups or solid phase binding groups" indicates **either** "1-10 hapten molecules and 1-10 marker groups" **or** "solid phase binding groups" **or instead** indicates "1-10 hapten molecules" **and** "1-10 marker groups or solid phase binding groups" (i.e., e.g., the instant specification at page 5, lines 25-28, states that "when using the conjugate according to the invention that contain 1-10 hapten molecules **and** a defined number of marker or solid phase binding groups as antigens . . . "); applicants are requested to point to where in the specification that term is defined. Clarification is requested.

Status of Claims

33. No claims are allowed in the instant application.

Conclusion

34. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Grace C. Hsu, Ph.D., J.D. whose telephone number is (703) 308-7005. The Examiner may be reached during normal business hours, Monday through Friday from 8:30 am to 5:30 pm (EST). A message may be left on the Examiner's voice mail.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Jythosna Venkat, Ph.D., may be reached at (703) 308-2439. The fax number assigned to Group 1627 is (703) 305-4242. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1627 receptionist whose telephone number is (703) 308-0196.

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